SYNDROME IDENTIFICATION CASE REPORT 131

ANOPHTHALMIA, MICROCEPHALY, HYPOTONIA, HYPOGONADISM, FAILURE TO THRIVE, AND DEVELOPMENTAL DELAY

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ABSTRACT

We describe a male child with multiple anomalies, including anophthalmia of one eye and microphthalmia with corneal opacities of the other, hypogonadism hypotonia, failure to thrive, developmental delay, and cardiac defects.

KEYWORDS: microphthalmia, cardiac defects, corneal opacities

INTRODUCTION

We describe a boy with anophthalmia of one eye and microphthalmia with corneal opacities and a coloboma of the other. He also had multiple congenital anomalies. His older sister (Fig. 1), who died at the age of 2 years, also had similar features. We have not come across a similar combination of anomalies in a child or in the literature before. The only photographs released by the parents are included.

HISTORY

This male Saudi child was born to a 20-year-old mother and a 30-year-old father after a 36-week gestational period. The birth weight was 1.2 kg, and length and head circumference were below the 3rd percentile for age. At birth, multiple congenital anomalies were noted, along with severe respiratory distress. He was ventilated for a period of 3 weeks with high pressures and high concentations of inspired oxygen.

There was no history of drug or alcohol use, fever, uterine infection, or illness during the pregnancy. The father had also been well. However, the parents were second cousins (Fig. 2). They had previously had a daughter (their only other child) with similar features (Fig. 1); she died at age 2 years. The cause of her death was not known.

PHYSICAL FINDINGS

At age 3 weeks the boy weighed 1.5 kg (< 3%), length was 46 cm (< 3%), and occipitofrontal circumference (OFC) was 28 cm (< 3%). He had right anophthalmia, with no evidence of a rudimentary eye. His left eye had a coloboma of the iris at 7 o'clock extending to the corneal limbus. The left pupil reacted to light, and the lens appeared normal. There were some direct attachments of the iris to the peripheral cornea superiorly, suggestive of focal iridocorneal dysgenises. The retina and optic disc in the left eye were normal. There were brief episodes of unsustained nystagmus in the left eye.

The other anomalies present were microcephaly, with large anterior and posterior fontanalle; low-set, simple, slanting ears, highly arched palate, and hypoplastic mandible. He had hypertelorism, with slight asymmetry of the face and thicker eyebrows on the right side. The wrists were held in flexion, with adducted thumbs and overriding of fingers and toes. The muscle tone was hypotonic and the genitalia were small and the testes undescended. Cardiac examination revealed a systolic

Fig 1. Sib at birth. Note bilateral microphthalmia, broad nose, and flexion deformity of the wrist.

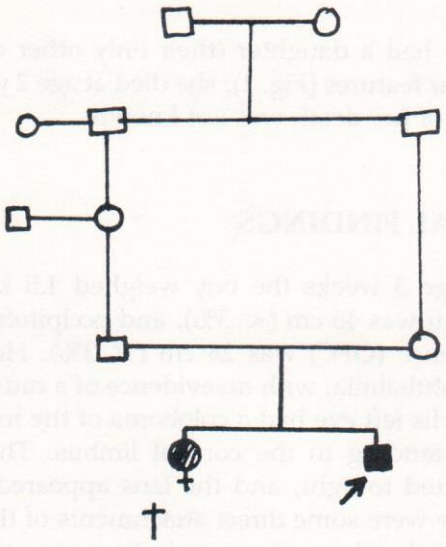

Fig 2. Family tree. Arrow shows proband.

murmur suggestive of pulmonary stenosis with ventricular septal defect (VSD).

Most recently, he was seen at age 2 years. He was not thriving, with length, weight, and OFC remaining below the 3rd percentile, but he seemed to have improved tremendously in that he was sitting, saying monosyllables like ma ma, ba ba. His intellectual and motor development corresponded to an infant of age 10 months (chronological age of 20 months).

The following anomalies were persistent: prominent forehead (Fig. 3) with large anterior fontanelle; failure to thrive [weight of 6.8 kg (< 3%), OFC of 42.9 (<3%), length of 69.4 cm (< 3%); absence of teeth; short, stubby nose; and mild overriding of fingers and toes. He was able to hear and with the help of eyeglasses was able to see objects at 3 feet.

LABORATORY AND X-RAY DATA

Blood, chemistry, and routine amino acid screening were all normal. Chromosome analysis showed a 46,XY karyotype. Computerized tonography scan of the brain and IV pyelogram were essentially normal. X-rays of the skull and face showed microcephaly, hypotastic mandibles, and small right orbit.

DISCUSSION

A number of syndromes were considered in the differential diagnosis because of the multiple anomalies present. Chromosomal abnormalities such as trisomy 18q-S, 13q-S, 4p-S, triploidy, and trisomy 13-S were excluded by the normal karyotype.

Fig 3. Proband at age 2 years. Note anophthalmia of the right eye, microphthalmia of the left eye, low-set simple ears, hypertelorism, prominent forehead, and bushy hair. He is unable to bear weight.

Varying degrees of microphthalmia along with coloboma have been reported in Goltz Syndrome, [1] but in our case, other than microphthalmia, coloboma, and no eruption of teeth, there were no other features of this syndrome. The nearest we could come was the CHARGE Association described by Hall in 1979.[2] In this association, many similar anomalies were noted in patients initially seen for ocular coloboma.[3]

Pagon et al. [4] introduced the acronym CHARGE association for coloboma, heart disease, atresia chonae, retarded growth and development and/or CNS anomalies, genital anomalies, and/or hypogonadism and ear anomalies and/or deafness. Since then, other anomalies have been included[5] to broaden the spectrum of this association even further.

Choanal atresia, which has been described in a large number of cases of CHARGE association, was not present in our case, and the heart defect, possibly a VSD, had closed by age 2 years. Deafness is reported to occur in 88% of patients with CHARGE association[5] but was not present in our case as determined from auditory evoked potentials.

Some of his other features, such as overriding of fingers and toes, hypotonia, large anterior and posterior fontanalle, and absence of teeth, have not been reported with CHARGE association. The sister who died at age 2 years (Fig. 1) had all these features plus arthrogryposis of all four limbs and a cleft palate, but arthrogryposis is a feature not described with CHARGE association.

The etiology of CHARGE association is not known, but it has been attributed to arrested development between days 35 and 45 post conception. We report this case and comment on his sib (not seen by us) to question whether these are indeed cases of CHARGE association. If they are, then by describing newer anomalies we wish to extend the spectrum of this association further. If they are not, then we report them as cases for syndrome identification.

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